

USSN: 10/052,798
Examiner: O'Hara
Art Unit: 1646

AMENDMENT TO THE CLAIMS

- Claims 1-58 and 63-64 have previously been cancelled.
- Claims 59-62 and 65-97 were previously pending.
- Please add new claims 98-146.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-58 (cancelled).

59. (previously presented) A method of inducing apoptosis in mammalian cancer cells comprising exposing mammalian cancer cells to an effective amount of monoclonal antibody which (a) binds to Apo-2 polypeptide consisting of the contiguous amino acid residues 1 to 411 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cancer cell *in vivo* or *ex vivo*.

60. (previously presented) The method of claim 59 wherein said antibody comprises a single-chain antibody.

61. (previously presented) A method of treating mammalian cancer cells comprising exposing mammalian cancer cells to an effective amount of monoclonal antibody which (a) binds to Apo-2 polypeptide consisting of the contiguous amino acid residues 1 to 411 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cancer cell *in vivo* or *ex vivo*.

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

62. (previously presented) The method of claim 61 wherein said antibody comprises a single-chain antibody.

Claims 63 and 64 (cancelled).

65. (previously presented) A method of inducing apoptosis in mammalian cancer cells comprising exposing mammalian cancer cells to an effective amount of monoclonal antibody which (a) binds to a soluble extracellular domain sequence of an Apo-2 polypeptide consisting of amino acids 54 to 182 SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.

66. (previously presented) A method of inducing apoptosis in mammalian cancer cells comprising exposing mammalian cancer cells to an effective amount of monoclonal antibody which (a) binds to a soluble extracellular domain sequence of an Apo-2 polypeptide consisting of amino acids 1 to 182 of SEQ ID:1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.

67. (previously presented) A method of treating mammalian cancer cells comprising exposing mammalian cancer cells to an effective amount of monoclonal antibody which (a) binds to a soluble extracellular domain sequence of an Apo-2 polypeptide consisting of amino acids 54 to 182 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.

68. (previously presented) A method of treating mammalian cancer cells comprising exposing mammalian cancer cells to an effective amount of monoclonal antibody which (a) binds to a soluble extracellular domain sequence of an Apo-2 polypeptide consisting of amino

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

acids 1 to 182 of SEQ ID NO: 1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.

69. (previously presented) The method of claim 59, 65, or 66, wherein said antibody is a chimeric antibody.

70. (previously presented) The method of claim 59, 65, or 66, wherein said antibody is a humanized antibody.

71. (previously presented) The method of claim 59, 65, or 66, wherein said antibody is a human antibody.

72. (previously presented) The method of claim 59, 65, or 66, wherein said antibody comprises an Fab fragment.

73. (previously presented) The method of claim 59, 65, or 66, wherein said antibody comprises a scFv fragment.

74. (previously presented) The method of claim 59, 65, or 66, wherein said antibody comprises a F(ab')₂ fragment.

75. (previously presented) The method of claim 59, 65, or 66, wherein said antibody binds to the same epitope as the epitope to which the monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number HB-12456 binds.

76. (previously presented) The method of claim 59, 65, or 66, wherein said antibody comprises one or more complementary determining region (CDR) amino acid sequences of the 16E2 antibody shown in Figure 16 (SEQ ID NO:9).

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

77. (previously presented) The method of claim 59, 65, or 66, wherein said antibody comprises one or more complementary determining region (CDR) amino acid sequences of the 20E6 antibody shown in Figure 16 (SEQ ID NO:10).
78. (previously presented) The method of claim 59, 65, or 66, wherein said antibody comprises one or more complementary determining region (CDR) amino acid sequences of 24C4 antibody shown in Figure 16 (SEQ ID NO:11).
79. (previously presented) The method of claim 59, 65, or 66, wherein said antibody is fused to an epitope tag sequence.
80. (previously presented) The method of claim 59, 65, or 66, wherein the cancer cells are colon or colorectal cancer cells.
81. (previously presented) The method of claim 59, 65, or 66, wherein the cancer cells are lung cancer cells.
82. (previously presented) The method of claim 59, 65, or 66, wherein the cancer cells are breast cancer cells.
83. (previously presented) The method of claim 61, 67, or 68, wherein said antibody is a chimeric antibody.
84. (previously presented) The method of claim 61, 67, or 68, wherein said antibody is a humanized antibody.
85. (previously presented) The method of claim 61, 67, or 68, wherein said antibody is a human antibody.

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

86. (previously presented) The method of claim 61, 67, or 68, wherein said antibody comprises an Fab fragment.

87. (previously presented) The method of claim 61, 67, or 68, wherein said antibody comprises a scFv fragment.

88. (previously presented) The method of claim 61, 67, or 68, wherein said antibody comprises a F(ab')₂ fragment.

89. (previously presented) The method of claim 61, 67, or 68, wherein said antibody binds to the same epitope as the epitope to which the monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number HB-12456 binds.

90. (previously presented) The method of claim 61, 67, or 68, wherein said antibody comprises one or more complementary determining region (CDR) amino acid sequences of the 16E2 antibody shown in Figure 16 (SEQ ID NO:9).

91. (previously presented) The method of claim 61, 67, or 68, wherein said antibody comprises one or more complementary determining region (CDR) amino acid sequences of the 20E6 antibody shown in Figure 16 (SEQ ID NO:10).

92. (previously presented) The method of claim 61, 67, or 68, wherein said antibody comprises one or more complementary determining region (CDR) amino acid sequences of the 24C4 antibody shown in Figure 16 (SEQ ID NO:11).

93. (previously presented) The method of claim 61, 67, or 68, wherein said antibody is fused to an epitope tag sequence.

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

94. (previously presented) The method of claim 61, 67, or 68, wherein said mammalian cancer cells are exposed to chemotherapy or radiation therapy.

95. (previously presented) The method of claim 61, 67, or 68, wherein the cancer cells are colon or colorectal cancer cells.

96. (previously presented) The method of claim 61, 67, or 68, wherein the cancer cells are lung cancer cells.

97. (previously presented) The method of claim 61, 67, or 68, wherein the cancer cells are breast cancer cells.

98. (New) A method of inducing apoptosis in mammalian cells expressing Apo-2 receptor comprising exposing mammalian cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody, wherein said antibody stimulates apoptosis in said mammalian cells upon its binding to said Apo-2 receptor, and wherein said antibody binds to an Apo-2 receptor polypeptide having at least about 80% sequence identity to SEQ ID NO:1.

99. (New) The method of claim 98 wherein said Apo-2 agonist antibody is a monoclonal antibody.

100. (New) The method of claim 98 wherein said agonist antibody is a chimeric antibody.

101. (New) The method of claim 98 wherein said agonist antibody is a humanized antibody.

102. (New) The method of claim 98 wherein said agonist antibody is a human antibody.

103. (New) A method of treating cancer, comprising exposing mammalian cancer cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody, wherein said antibody stimulates apoptosis in said cells upon its binding to said Apo-2 receptor, and wherein

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

said antibody binds to an Apo-2 receptor polypeptide having at least about 80% sequence identity to SEQ ID NO:1.

104. (New) The method of claim 103, wherein said cancer cells are lung cancer cells.
105. (Original) The method of claim 103, wherein said cancer cells are colon cancer cells.
106. (Original) The method of claim 103, wherein said cancer cells are glioma cells.
107. (New) A method of inducing apoptosis in mammalian cells expressing Apo-2 receptor comprising exposing mammalian cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody which (a) binds to Apo-2 polypeptide consisting of the contiguous amino acid residues 1 to 411 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.
108. (New) The method of claim 107 wherein said Apo-2 agonist antibody is a monoclonal antibody.
109. (New) The method of claim 107 wherein said agonist antibody is a chimeric antibody.
110. (New) The method of claim 107 wherein said agonist antibody is a humanized antibody.
111. (New) The method of claim 107 wherein said agonist antibody is a human antibody.
112. (New) The method of claim 107 wherein said mammalian cells expressing Apo-2 receptor are cancer cells.
113. (New) The method of claim 112 wherein said cancer cells are lung cancer cells.
114. (New) The method of claim 112 wherein said cancer cells are colon cancer cells.
115. (New) The method of claim 112 wherein said cancer cells are glioma cells.

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

116. (New) A method of inducing apoptosis in mammalian cells expressing Apo-2 receptor comprising exposing mammalian cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody which (a) binds to a soluble extracellular domain sequence of an Apo-2 polypeptide which consists of amino acid residues 54 to 182 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.
117. (New) The method of claim 116 wherein said Apo-2 agonist antibody is a monoclonal antibody.
118. (New) The method of claim 116 wherein said agonist antibody is a chimeric antibody.
119. (New) The method of claim 116 wherein said agonist antibody is a humanized antibody.
120. (New) The method of claim 116 wherein said agonist antibody is a human antibody.
121. (New) The method of claim 116 wherein said mammalian cells expressing Apo-2 receptor are cancer cells.
122. (New) The method of claim 121 wherein said cancer cells are lung cancer cells.
123. (New) The method of claim 121 wherein said cancer cells are colon cancer cells.
124. (New) The method of claim 121 wherein said cancer cells are glioma cells.
125. (New) A method of treating cancer, comprising exposing mammalian cancer cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody which (a) binds to Apo-2 polypeptide consisting of the contiguous amino acid residues 1 to 411 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cancer cell *in vivo* or *ex vivo*.
126. (New) The method of claim 125 wherein said Apo-2 agonist antibody is a monoclonal antibody.
127. (New) The method of claim 125 wherein said agonist antibody is a chimeric antibody.

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

128. (New) The method of claim 125 wherein said agonist antibody is a humanized antibody.
129. (New) The method of claim 125 wherein said agonist antibody is a human antibody.
130. (New) The method of claim 125 wherein said mammalian cancer cells are lung cancer cells.
131. (New) The method of claim 125 wherein said mammalian cancer cells are colon cancer cells.
132. (New) The method of claim 125 wherein said mammalian cancer cells are glioma cells.
133. (New) A method of treating cancer, comprising exposing mammalian cancer cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody which (a) binds to a soluble extracellular domain sequence of an Apo-2 polypeptide which consists of amino acid residues 54 to 182 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cell *in vivo* or *ex vivo*.
134. (New) The method of claim 133 wherein said Apo-2 agonist antibody is a monoclonal antibody.
135. (New) The method of claim 133 wherein said agonist antibody is a chimeric antibody.
136. (New) The method of claim 133 wherein said agonist antibody is a humanized antibody.
137. (New) The method of claim 133 wherein said agonist antibody is a human antibody.
138. (New) The method of claim 133 wherein said mammalian cancer cells are lung cancer cells.
139. (New) The method of claim 133 wherein said mammalian cancer cells are colon cancer cells.
140. (New) The method of claim 133 wherein said mammalian cancer cells are glioma cells.
141. (New) The method of claim 98 wherein said Apo-2 receptor polypeptide has at least about 85% sequence identity to SEQ ID NO:1.

USSN: 10/052,798

Examiner: O'Hara

Art Unit: 1646

142. (New) The method of claim 98 wherein said Apo-2 receptor polypeptide has at least about 90% sequence identity to SEQ ID NO:1.
143. (New) The method of claim 98 wherein said Apo-2 receptor polypeptide has at least about 95% sequence identity to SEQ ID NO:1.
144. (New) The method of claim 103 wherein said Apo-2 receptor polypeptide has at least about 85% sequence identity to SEQ ID NO:1.
145. (New) The method of claim 103 wherein said Apo-2 receptor polypeptide has at least about 90% sequence identity to SEQ ID NO:1.
146. (New) The method of claim 103 wherein said Apo-2 receptor polypeptide has at least about 95% sequence identity to SEQ ID NO:1.